

Remarks

In response to the Final Rejection of April 5, 2006, Applicants enclose an Amendment and an Information Disclosure Statement (IDS). By virtue of the filing of a Request for Continued Examination submitted herewith, the enclosed Amendment and IDS are now entered into the application. Favorable consideration of this application is respectfully requested in view of the above amendment and following remarks.

Claims 28-46 and 48-55 are pending in the application. Claims 40, 43, and 50-54 have been withdrawn. Claims 28-39, 41, 42, 44-46, 48, 49 and 55 have been rejected. Claims 28, 29 and 48 have been amended.

Claims 28, 30, 31, 36, 41, 42, 44-46, 49 and 55 have been rejected under 35 U.S.C. §102(b) as being unpatentable by Carpino et al., (J. Org. Chem. 1999, 64, 4324-4338, referred herein as Carpino et al.) as allegedly evidenced by Solomons et al., (Organic Chemistry Fifth Edition. New York: John Wiley & Sons, 1992, page 94, Table 3.1) and Lide (CRC Handbook of Chemistry and Physics, ed. DA Lide, 85th Edn., CRC Press, Cleveland OH, 2004-2005, web page 1.) In particular, the Examiner stated *inter alia*:

Carpino et al. also disclose at least one step (b), referred to as step (b'), in which an amine comprising a free anion or a latent anion is used as a scavenger of residual activated carboxylic acid (e.g., see page 4329, column 1, first paragraph wherein "ethanolamine" is disclosed). The reference does not state that ethanolamine possesses a "free anion or latent anion", but the examiner contends that this would be an inherent property of ethanolamine via the following equilibrium in water $\text{NH}_2\text{CH}_2\text{CH}_2\text{OH} \leftrightarrow \text{NH}_2\text{CH}_2\text{CH}_2\text{O}^- + \text{H}^+$ (e.g., see Lide, web page 1, "Dissociation Constants of Organic Acids and Bases" section, Ethanolamine entry wherein $\text{pK}_a = 9.5$; see also Solomons, page 94, Table 1, wherein pK_a of water = 15.74) "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not."....

Applicants respectfully disagree with the Examiner's assertions and conclusion and submit that independent claim 28 is not anticipated by Carpino et al. as allegedly evidenced by Solomons and Lide for the reasons stated below.

Applicants assert that the pK_a value of 9.5 for ethanolamine refers to the protonation of ethanolamine (equilibrium between $\text{NH}_3^+\text{CH}_2\text{CH}_2\text{OH}$ and $\text{NH}_2\text{CH}_2\text{CH}_2\text{OH}$), while the pK_a value of 16 refers to the dissociation of ethanolamine (equilibrium between $\text{NH}_2\text{CH}_2\text{CH}_2\text{OH}$ and $\text{NH}_2\text{CH}_2\text{CH}_2\text{O}^-$). The latter is indeed the equilibrium that is of importance for the DioRaSSP[®] invention, *i.e.* the anion formation that plays a crucial role in the removal of quenched compounds within the protocol of the present invention. In fact, within the quenched compounds the amine function of ethanolamine would not even be present as such; rather, at the stage of the

aqueous extractions, it has been acylated by the activated carboxylic compound to yield an ethanolamide function of a considerably higher pK_a value.

Assuming that peptide synthesis would allow the application of pH values of approximately 15.74, dissociation and thus active extractive removal of quenched compounds would still be an equilibrium and therefore incomplete. However, it is also known to a person skilled in the art, that peptide synthesis is not compatible with such strongly basic (aqueous) conditions, which would result in not merely destruction of the peptide, but also of the preferred solvent of the present invention (ethyl acetate). The pH value during peptide synthesis should not exceed a pH value of approximately 12, corresponding to a dissociation extent of the ethanolamide function of 0.01 %.

It is further asserted that Carpino et al. fail to teach one skilled in the art that the alcohol moiety of the ethanolamide function is an anion that can be used as a scavenger. Instead, Carpino et al. teach that the alcohol moiety of the ethanolamide function remains intact during aqueous washings and does not form an anion. This assertion is underlined by the fact that extractions within the Carpino protocol are performed at neutral pH corresponding to a dissociation extent of the ethanolamide function of 10^{-7} %. Accordingly, the ethanolamide function in the presence of aqueous washings as is described in Carpino et al. would not function as a scavenger as is recited in claim 28.

In view of the above, withdrawal of the rejection of claims 28, 30, 31, 36, 41, 42, 44-46, 49 and 55 under 35 U.S.C. §102(b) is respectfully requested.

Claims 28-31, 36, 41, 42, 44-46, 48, 49 and 55 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Carpino et al., WO 00/71569 (Tolle et al.) and Houghten et al., Nature 1991, 354, 84-86 (Houghten et al.). Applicants respectfully disagree with the Examiner's conclusion and submit that the combination of references does not make obvious independent claim 28.

The arguments proffered above to address the §102 rejection apply equally well to this rejection, namely that at such high pH values, i.e., pH 16, peptide synthesis would not be compatible with such strongly basic conditions and would result in the destruction of the peptide. Further, extractions at a neutral pH as is described in Carpino et al. would correspond to a dissociation extent of the ethanolamide function of 10^{-7} % and thus the alcohol moiety of ethanolamide function would remain intact following the protocol of Carpino et al. Accordingly, the ethanolamide function subjected to aqueous washings at a neutral pH as described by Carpino et al. would not function as a scavenger as recited in claim 28. In addition, neither Tolle et al. or Houghten et al. describe an amine comprising a free anion or latent anion that could function as a

scavenger as recited in claim 28, and thus Tolle et al. and Houghten et al. do not remedy the deficiencies present in Carpino et al.

In view of the above, withdrawal of the rejection of claims 28-31, 36, 41, 42, 44-46, 48, 49 and 55 under 35 U.S.C. §103(a) is respectfully requested.

Claims 53 and 54 have been provisionally rejected under 35 U.S.C. §101 as allegedly claiming the same invention as claims 43 and 44 of copending application No. 10/692,354 (2004/0082760A1).

In response, Applicants note that these claims were previously withdrawn.

In view of the above, withdrawal of the rejection of claim 53 and 54 as allegedly claiming the same invention as claims 43 and 44 of copending application No. 10/692,354 is respectfully requested.

Claims 28-39, 41, 42, 44-46, 48, 49, 51, 52 and 55 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 28-51 of copending Application No. 10/692,354.

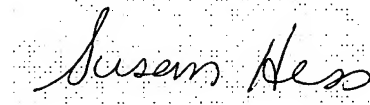
In response, Applicants will address the obviousness-type double patenting rejection upon indication that claim 28 is deemed to be allowable except for the obviousness-type double patenting rejection.

Claim 28 has been objected to as allegedly containing an informality, i.e., the recitation of "and" twice in step (c). In response, claim 28 has been amended to delete one "and".

In view of the above, withdrawal of the objection of claim 28 is respectfully requested.

A good faith effort has been made to place the present application in condition for allowance. If the Examiner believes a telephone conference would be of value, he is requested to call the undersigned at the number listed below.

Respectfully submitted,



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